

THE CLINICAL SIGNIFICANCE OF NUTRITIONAL DEFICIENCIES IN PREGNANCY*

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FOR too long a time pregnancy has been considered a normal physiological function occupying a nine months interim at some time or times during a patient's child-bearing years. Fortunately, present day concepts of nutrition have shed new light, making possible a different interpretation, on what should be considered normal physiology. Undoubtedly, pregnancy should be a normal physiological function in the human female, but we rarely see a patient whose physiological response to pregnancy can be considered normal. It would then appear that our base line of normal has been established against patients who are sub-normal to begin with. For years, our attention has been concerned with the various catastrophes of pregnancy *after* these catastrophes have occurred, yet these observations have shed little light on the underlying causative or preventive factors.

Consequently, in 1935, we undertook to evaluate by clinical observations, the effect of improved nutrition on maternal and infant well-being. Our initial efforts were directed toward establishing a minimum optimum diet for pregnancy, one which would, of course, provide an adequate caloric value, estimated on the basis of the patient's weight at the beginning of pregnancy and her energy requirements. But of greater importance, one which would supply necessary amounts of animal and non-animal protein, carbohydrates and fats, and at least minimal protective amounts of the known vitamins and minerals. Since the average weight at the beginning of pregnancy, among the patients registered in the Prenatal Clinic at the Philadelphia Lying-in Hospital, was found to be 129 pounds, our standardized diet was arbitrarily established on this weight basis. It contains approximately 2200 calories, consisting of 110 grams of protein (of which approximately 80 grams

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are animal protein), 85 grams of fat and approximately 300 grams of carbohydrates. Every effort has been made to maintain a practical and palatable diet—one which a patient could be expected to eat. A theoretically ideal diet might be considerably different from one which is practical and optimum.

The success which we have had with improved nutrition in our research group of patients has been dependent upon several factors, among which are:

The patients attending the Research Clinic have been given intensive and persistent dietary instructions, both written and oral. It should be emphasized that this is primarily the physician's responsibility, and that only by individual dietary analysis, investigation of the patient's dietary habits and the specific correction of the dietary errors noted, can adequate results be obtained. The simple expedient of giving the patient a printed dietary outline, or telling her to eat a "well-balanced" diet, is ridiculous on the face of it.

Six small meals a day, at approximately three-hour intervals, have been found to be essential; and we have found a marked improvement will result in all patients if this regime of interval feeding is adhered to. Such a regime has been found to decrease markedly the severity of nausea and vomiting during early pregnancy, and to aid in the elimination of fatigue and other symptoms associated with energy depletion. The gastro-intestinal tract becomes hypotonic surprisingly early in pregnancy, and unless adequate measures are instituted immediately, this dysfunction will continue or become exaggerated and will result in a failure of intestinal absorption with resulting maternal and fetal shortages. It further aids in decreasing the intake of a high caloric carbohydrate diet by maintaining an active appetite which can be readily satisfied with the essential food elements without the uncontrollable desire on the part of many patients to substitute restricted items for required items of food.

There are excessive metabolic demands of pregnancy during the first trimester, or formative period of the fetus, and particularly during the third trimester, the period of most rapid growth and development. This makes it essential that there be an adequate caloric intake, and that it include sufficient energy producing and tissue protective foods to answer the patient's increased nutritional and metabolic requirements.

It has been stated that patients will not coöperate on such a regime.

We have not found this to be the case. Granted, it required persistent personal supervision and instructions to accomplish, but a most satisfactory response can be obtained once the interval regime has been established, except for those isolated patients who are unable to understand, who cannot for some vague reason conform, or those few who refuse to coöperate. We have yet to have a patient who has not frankly admitted an improvement in her general well-being after being on this schedule for a short time.

It should be noted that fruit and fruit juices have been restricted to two servings daily. Excessive ingestion of fruit and fruit juices, entailing intake of large amounts of fluid and sugar, has been found to be one of the more important dietary errors associated with the initiation of excessive gain in weight and edema, since in the majority of cases, the correction of this one dietary error aided materially in the elimination of these problems. Excess gain in weight and resulting edema usually do not result solely from the excessive ingestion of fruit and fruit juices, but because the patient takes these foods instead of adequate amounts of protein, thus materially increasing her caloric intake plus upsetting her protein-carbohydrate ratio. This error usually begins early in pregnancy, and initiates or furthers, a state of hypoproteinemia which we believe to be one of the primary causes of edema associated with pregnancy. It should be stressed that constant effort must be directed toward establishing an adequate intake of protein and that essentially pure carbohydrate foods are to be taken in addition to or after, not instead of, the essential foods necessary to the maintenance of normal physiology and metabolism.

Fluids have been restricted to a level of normal fluid balance, aiding materially in avoiding the tendency on the part of many patients to substitute fluids for adequate food. We believe that excessive retention of fluid can better be controlled by proper intake of food, rather than through excessive restriction of fluid or dehydrating measures.

We instruct our patients to restrict their total fluid intake to eight glasses a day. This has frequently been questioned as being an inadequate amount of fluid. Anyone who will take the time to observe and investigate the normal fluid balance level of a large group of patients, will find that patients in optimum physiological balance will be completely satisfied at this level, and will not show evidence of fluid retention. We have yet to see a patient with persistent edema whose fluid

intake did not exceed this level by at least 50 per cent or more. It has been our experience that fluid intake above the 64-ounce level is not at any time necessary. No doubt, many patients can stabilize on a fluid intake in excess of this, but for practical working purposes, experience has shown this to be an advisable level for an arbitrary base line. Obviously, all patients are not alike, and again individualization of each patient's requirements must be established.

It has been our experience that the majority of patients who show evidence of excessive fluid or fruit intake, have been substituting fluid or fruit for proper food. We believe that this has often resulted from errors in instruction by those responsible for nutritional advice, who do not realize that this is one situation where fruit is not a panacea.

Except where excessive salt intake is demonstrated, the restriction of salt has been found unnecessary. The primary object of this program is to obtain the patient's coöperation in eating correctly. As a diet with a moderate amount of salt is more palatable, the patient is more likely to follow instructions than were she advised to eat a salt-free diet. Since it is almost impossible to produce a diet with less than approximately 2.5 grams of salt and still retain palatability, a diet with less than this level is not considered feasible, or desirable. In individual instances in which toxemia has developed with evidence of edema, the problem immediately becomes one of major disturbance and must be individualized on the basis of the entire clinical picture, rather than the simple expedient of salt restriction. Among patients under positive nutritional control, this has not been a problem.

Our instructions to patients to refrain from eating pastry, ice-cream, candy and nuts, have been questioned as being a ridiculous request to make of any woman during pregnancy. In working with large groups of patients certain standards must be established, and it has been found that the above advice is essential, and except in isolated cases, has not produced any hardship or lack of coöperation on the part of our patients once the reason for this restriction is understood. Patients who are coöperating and are satisfactorily stabilized, are permitted occasional small amounts of the restricted items, but they are carefully instructed that these, as well as many other items of food, may be taken only after all other essential nutrients have been taken, never instead of. We have not found this to be a problem, and a majority of our patients have voluntarily stated that after being on the advised dietary, they

no longer have a great desire for ice cream, pastries and sweets.

The caloric requirements during pregnancy can not be arbitrarily stated for all patients. As stated above, we have established our specific dietary instructions on the basis of a beginning pregnancy weight of 129 pounds which we have found to be average. Obviously, patients weighing 90 pounds or 175 pounds at the beginning of pregnancy will require an entirely different caloric intake to maintain optimum gain in weight during their pregnancy. To answer the necessary energy requirements, diets containing 1600 calories or less, which have appeared in the literature from time to time, cannot possibly supply optimum or essential nutrients; and diets containing 3,000 or more calories are in excess of the caloric requirements for the average patient.

To repeat—the simple expedient of handing the patient a printed dietary outline is of no value in a long range nutritional program. Few, if any, patients understand the real reason for nutritional reinforcements during pregnancy, and they are entitled to complete and detailed individualized dietary instructions from their doctor.

The degree of nutritional adequacy at the beginning of pregnancy will determine the degree of deficiency which can be expected to develop should dietary habits remain unchanged. In other words, a patient whose nutrition is adequate at the beginning of pregnancy, and who maintains an adequate dietary regime, is better able to withstand the depleting effects of early nausea and vomiting and the increasing metabolic demands of late pregnancy without marked disturbance. On the other hand, the patient who begins her pregnancy showing definite signs and/or symptoms of deficiency, and whose nutritional intake continues to be inadequate, will show increasing degrees of distress, depending on the severity and velocity of the nutritional inadequacy. Our observations support the idea that the fetus obtains its nutritional requirements prior to the maternal organism, and draws upon maternal storages. When these storages are depleted to a point of deficiency in the mother, the baby will fail to obtain the necessary elements.

Some statistics showing the results of improved maternal and fetal nutrition illustrate the clinical significance of nutritional deficiencies in pregnancy. The results for the patients in the Research Group may be compared with those of the Control Group in that emergency admissions and others who had not registered for care in advance and had not made two or more prenatal visits have been excluded. All non-viable

TABLE I: STATISTICAL DATA

	<i>Research Group (593)</i>		<i>Control Group (772)</i>		<i>% Increase</i>
	<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>	
Total Baby Deaths	11	1.85	18	2.33	26
Stillbirths	5	0.84	9	1.16	38
Neonatal Deaths	6	1.01	9	1.16	15
Prematurity	24	4.16	54	7.07	70
Pre-Eclampsia	0	0	12	1.56	—
Eclampsia	0	0	1	0.13	—

1. Total baby deaths were 18 in the control group and 11 in the research group, or an increased incidence of 26 per cent in the Control Group over the Research Group.
2. In the Research Group, there were only five stillbirths and six neonatal deaths or 0.84 per cent and 1.01 per cent respectively. Among the 772 control patients, there were nine stillbirths and nine neonatal deaths, or 1.16 per cent and 1.16 per cent respectively, which represents an increased incidence in the Control Group of 38 per cent for stillbirths and 15 per cent for neonatal deaths.
3. Pre-eclampsia and eclampsia did not occur in the Research Group, where in the Control Group, there was an incidence of 12 cases or 1.56 per cent of pre-eclampsia and 1 case or 0.13 per cent of eclampsia.
4. There were 54 prematures in the Control Group and 24 in the Research Group, or an increased incidence of 70 per cent in the Control Group.

TABLE II: INCIDENCE OF OBJECTIVE AND SUBJECTIVE OBSERVATIONS

	<i>No. of Patients</i>	<i>% of Patients</i>
Total	165	100.0
Glossitis	162	98.2
Gums	136	82.4
Cheilosis	5	3.0
Stomatitis	5	3.0
Fatigue	115	69.7
Legs, Weakness, Pain	90	54.5
Gastro-Intestinal Hypotonia	85	51.5
Weakness	74	44.8
Anorexia	73	44.2
Constipation	61	37.0
Dyspnea & Palpitation	60	36.4
Irritability	53	32.1
Arms & Hands, Weakness, Pain	33	20.0
Burning of Feet	32	19.4
Insomnia	28	17.0
Muscular Weakness	19	11.5

infant deaths as well as all colored patients have also been excluded from both groups.

Data for the control group have been compiled from the year 1939, a period about the middle of the years included in the study.

VITAMIN DEFICIENCIES

We have been able to demonstrate signs and/or symptoms of nutritional deficiency, usually of the sub-clinical type, in at least 98 per cent of our patients.

Table II shows incidence of objective and subjective observations suggestive of nutritional deficiencies as found in patients of the present Nutrition Research Clinic.

Although nutritional deficiency of an advanced degree is comparatively uncommon in the Philadelphia area, sub-clinical states are by no means infrequent. The incidence of glossitis in 98 per cent of our patients and polyneuritis in at least 54 per cent clearly indicates the frequency of deficiency states of minor degree. The most commonly observed nutritional deficiency states are characterized clinically by evidence of vitamin deficiencies. The relationship between avitaminosis and the metabolism of other vital elements is not completely understood, except that for optimal metabolism adequate amounts of all essential food elements are necessary.

We have observed an incidence of sub-clinical scurvy in approximately 82 per cent of our patients. The gingivitis so commonly seen in pregnancy is usually attributed to an infection. It is true that infection is frequently present, but generally the underlying cause of the disturbance is a lack of Vitamin C.

Our observations show a much greater incidence of Vitamin A deficiency than has heretofore been suggested. Straumfjord states that vernix caseosa is a manifestation of deficiency of Vitamin A. This, together with other reported evidences, points to the fact that a high percentage of patients are lacking in adequate amounts of this factor.

The necessity for adequate amounts of the B-complex for satisfactory metabolism of protein and carbohydrates is well established, and the majority of the clinical observations of deficiency are characterized by evidence of a lack of these important vitamins.

Pregnancy demonstrates more readily than almost any other condition the fact that adequate intake of food in no way guarantees

optimum absorption, utilization or storage; yet it must be emphasized that it is essential to obtain the necessary nutritional elements from natural food sources, rather than from supplemental therapy alone.

The importance of vitamin supplementation is becoming more and more apparent as our clinical experience progresses, and further, such experience indicates that this supplementation should consist of a relatively high potency polyvitamin concentrate. Many workers have stated that the requirements for such factors as thiamin chloride, riboflavin, niacin and ascorbic acid are relatively low. Our observations clearly indicate that during pregnancy, the requirements for the known vitamins are comparatively high. This is especially true of the B-complex factors.

Throughout this study it has been observed that in many cases, a typical syndrome developed during the middle or latter part of the second trimester. This syndrome is characterized by fatigue, lassitude, mild depression and general physiological hypotonia. Frequently, this has appeared in patients known to be coöperating with our nutrition advice. With the advent of parenteral B-complex, patients of this type have made a prompt and satisfactory response to therapy, where previously they responded poorly if at all. This strongly suggests that even these apparently well stabilized individuals may fail to adequately absorb or utilize a well planned and optimum diet. It further demonstrates that in many cases there is an absolute necessity for parenteral polyvitamin supplementation, in order to by-pass the oral route, to re-establish normal intestinal absorption and efficiency. The indication is that the primary breakdown responsible for the development of disturbances occurring in late pregnancy, is usually initiated by an absorptive failure in the gastrointestinal tract, rather than a utilization failure. It should be emphasized that in pregnancy, parenteral vitamin therapy is essential in acute deficiency states, and may be necessary even in the mild chronic types, in order to obtain a satisfactory nutritional balance throughout the remainder of pregnancy.

We have not used supplemental calcium therapy in the research group of patients, and do not believe that calcium in its present available supplemental form is of any value in the prevention of dental caries, or as a substitute for calcium from natural food sources.

At present, the only reliable means by which a patient's nutritional status can be evaluated is by clinical observations. Technical studies are

TABLE III: HEMOGLOBIN VARIATIONS AMONG 688 PATIENTS AT THE TIME OF ADMISSION TO PRENATAL CLINIC, PHILADELPHIA LYING-IN HOSPITAL, JULY 23, 1947 TO AUGUST 18, 1947.

<i>Hemoglobin in gram</i>	<i>Number of Patients</i>	<i>% of Total Patients</i>
9.0 or less	14	2.0
9.5 " "	41	5.9
10.0 " "	81	11.7
10.5 " "	168	24.4
11.0 " "	285	41.4
11.5 " "	368	53.5
12.0 " "	456	66.3
12.5 " "	548	79.7
13.0 " "	610	88.7
13.5 " "	643	93.5
14.0 " "	672	97.7
14.5 " "	685	99.6
15.0 " "	687	99.9
15.5 " "	688	100.0

as yet unreliable for this purpose and are of value only in dietary analysis, or in determining the patient's actual food intake. In establishing the nutritional status of patients attending the Nutrition Research Clinic, the objective and subjective evidences suggestive of nutritional inadequacy are evaluated. These findings then become the base line against which therapeutic management is formulated.

ANEMIAS OF PREGNANCY

Our observations indicate that supplemental iron therapy alone is of little value, and that iron deficiency anemias occurring in pregnancy are rare. Most of the anemias being typically nutritional anemias, do not respond to iron alone unless accompanied by an adequate diet and supplemented with vitamin and whole liver therapy. Recent observations suggest a more prompt and marked response when iron was omitted and whole desiccated liver substituted.

The variations in hemoglobin level shown in Table III are of probable significance. The hemoglobin determinations were derived from all patients attending the prenatal clinic at the Philadelphia Lying-In Hospital from July 23rd, 1947, to August 18th, 1947, and were taken on the first day of admission and therefore can be said to represent the

hemoglobin in the individual patient at the time she became pregnant. A further sampling of hemoglobins, at repeated visits, among 175 research clinic patients has not shown a single incidence of blood dyscrasia, macrocytic or microcytic anemia. Since all of these anemias represent a normocytic anemia, it seems rational to assume that they are entirely of nutritional origin, and further supports the thesis of the significance of sub-clinical nutritional deficiency states occurring early in pregnancy or existing at the time pregnancy occurs.

If we were to accept suggested standards of 10 grams of hemoglobin as the low limit of normal for hemoglobin during pregnancy, it would be to accept a standard too far below a level commensurate with maternal and fetal safety, oxygen requirements and general physiological adequacy.

Considerable emphasis is at present being placed upon the need for folic acid with the inference that it is a cure-all for the true or simple hypochromic anemias of pregnancy. Folic acid has not been demonstrated as being effective except in the presence of true macrocytic anemias. Since macrocytic anemias are rare in pregnancy, in most areas, the indications for folic acid as a routine, and especially as an isolated therapeutic adjunct, are also rare. Again it must be emphasized that the anemias of pregnancy, except in the presence of blood dyscrasias, are the result of a nutritional deficiency; that adequate natural food dietary corrections must first be established, and that the proper supplementation can only be determined after proper evaluation of the type of deficiency existing in the individual patient being considered. It is believed that adequate amounts of folic acid to supply the needs of most patients will be available if the basic dietary is adequate, and that folic acid will be required only in cases of prolonged deficiency or severe acute states.

Unquestionably, the demands of the baby and the increased metabolic load of the mother create a markedly increased demand for the various vitamins. We have been unable to establish any standard dosage since it depends entirely upon the nutritional status of the patient at the beginning of her pregnancy, her dietary habits throughout pregnancy, and the period of pregnancy under consideration. Our efforts, therefore, have been directed toward improving the patient's nutrition through natural food sources, and supplementing her improved diet with sufficient dosage of the various vitamins to control the signs and/or

symptoms of the observed deficiencies and the estimated additional requirements of the developing fetus.

Repeated dietary surveys among large groups of comparable patients show a protein intake averaging about 55 grams per day, and since hemoglobin averages as shown in Table III are consistent with these findings, it is becoming more and more apparent that hemoglobin levels have a direct correlation with protein intake levels. It is well established that hypoproteinemia is a major factor in the production of hydremia. Since secondary, or simple, anemias of pregnancy are usually stated to be the result of a physiological hydremia, it is our opinion that the high incidence of the secondary anemias of pregnancy are the result of a hypoproteinemia, and the associated general under-nutrition. We do not believe that the so-called physiological hydremia of pregnancy is normal, but is in fact evidence of hypoproteinemia, and will increase as the intake of protein decreases, or requirements for protein increase. Therefore, our efforts are directed early in pregnancy toward a primary improvement in the patient's basic dietary, rather than the useless administration of iron, or hematopoietic stimulants without consideration of essential nutritional requirements.

TOXEMIAS OF PREGANCY

We believe that the so-called toxemias of pregnancy are in reality a nutritional deficiency state. Since this condition constitutes one of the greatest hazards to the mother and baby, it has received a major portion of our attention. The fact that severe pre-eclampsia and eclampsia did not occur in the research group of patients, indicates these syndromes to be the result of a failure in maternal metabolism. This thesis is further supported by a marked decrease in the incidence of mild toxemia.

It is of considerable interest to us that in most patients with pre-eclampsia, the condition is readily reversible by means of nutritional therapy alone. This is particularly true if the onset of pre-eclampsia is recognized early and adequate nutritional therapy is immediately instituted. We believe the rate of gain in weight is the most important early clinical observation relative to the onset of pre-eclampsia. Patients adhering properly to our nutritional instructions, and maintaining a positive nutritional balance, have been found to maintain a weight curve characterized by either a plus or minus three pounds the first trimester.

Whether this is a plus or minus, ascending or descending curve, will be determined by the amount or severity of nausea and vomiting which occurs. The weight curve should rise one-half pound per week the second trimester, and one pound per week the third trimester, up to about the 37th or 38th week, at which time the weight usually remains constant, or slightly decreases.

During the second trimester, it is of critical significance if a patient gains two or three times as much as she should. For example, during the second trimester, the patient should gain two pounds per month, whereas many patients and doctors would attach little significance to a gain of four pounds during this period. However, this four pounds represents twice as much as the patient should have gained, and if this rate of gain is continued into the third trimester, no one would disagree that the patient's weight gain was in definite excess of optimum. Intensive efforts at nutritional stabilization should be instituted at any time during pregnancy that the gain in weight is excessive. Pre-eclampsia which has been allowed to continue even in a mild form, for a considerable period, will be found difficult to improve, and may even be irreversible. This strongly suggests a physiological breakdown in the patient's metabolic processes beyond a point commensurate with the comparative slowness of nutritional therapy instituted late in pregnancy. This further indicates the absolute necessity for early nutritional stabilization as a preventive measure, rather than waiting until after a catastrophe has occurred and then relying on emergency measures. We are adamant in our opinion that should personal instruction fail to produce immediate correction of early evidence of toxemia, the patient must be hospitalized, or in some other way made to re-establish an adequate nutritional status. We have found it to be more expedient to hospitalize our patients early for restabilization procedures of a preventive nature, than to wait until a severe catastrophe occurs which will require prolonged hospitalization, and not infrequently radical procedures to terminate the pregnancy.

PREMATURITY

The incidence of only 4.16 per cent of prematurities in the research group as contrasted with an incidence of 7.07 per cent in the control group, or an increased incidence of 70 per cent in the control group over the research group indicates the significance of adequate nutrition

in pregnancy particularly from the point of view of infant salvage. This same tendency towards increased birth weights above premature levels, occurring in conjunction with improved maternal nutrition has been verified by several other clinics.

INFANT MORTALITY

A decrease in stillbirths and neonatal deaths is undoubtedly effected by several factors in any clinic. However, an increased incidence in total infant mortality of 26 per cent in the control group, over the research group which had improved maternal nutrition, suggests that adequate amounts of nutritional elements have played a major part. Since the placenta is maternally nourished, it seems rational that many of the infant catastrophes can be ascribed to a nutritional failure in the placental bed; the result of an inadequate intake, or inability of the mother to supply the essential elements needed for placental storage and placental cellular function. Statistical data are not available as yet, but there is a definite indication that the infant salvage from stillbirths and neonatal deaths can be increased as our methods and techniques of maternal nutrition are improved.

Maternal nutrition is of equal or greater importance than any other service. That it can materially improve maternal and infant health, and provide for a reserve against the depleting effects occurring in pregnancy, seems obvious. Likewise, it should be most obvious that the betterment of the mother and infant, and the increasing of infant salvage, must commence not later than the beginning of pregnancy, rather than at some later date when it becomes apparent that the well-being of the newborn infant is substandard.